Applicant: Shohei Koide Attorney's Docket No.: 17027.003US1

Serial No.: 09/903,412 Filed: July 11, 2001

Page : 2 of 15

## **AMENDMENTS TO THE SPECIFICATION**

Please replace the first full paragraph on page 76 with the following amended paragraph:

The carboxyl triad (Asp 7 and 23, and Glu 9) is highly conserved in FNfn10 from nine different organisms that were available in the protein sequence databank at National Center for Biotechnology Information (www.ncbi.nlm.nih.gov). In these FNfn10 sequences, Asp 9 Asp 7 is conserved except one case where it is replaced with Asn, and Glu 9 is completely conserved. The position 23 is either Asp or Glu, preserving the negative charge. As was discovered in this study, the interactions among these residues are destabilizing. Thus, their high conservation, despite their negative effects on stability, suggests that these residues have functional importance in the biology of fibronectin. In the structure of a four-FN3 segment of human fibronectin (Leahy, D. J., Aukhil, I. & Erickson, H. P. (1996) Cell 84, 155-164), these residues are not directly involved in interactions with adjacent domains. Also these residues are located on the opposite face of FNfn10 from the integrin-binding RGD sequence in the FG loop (Figure 21). Therefore, it is not clear why these destabilizing residues are almost completely conserved in FNfn10. In contrast, no other FN3 domains in human fibronectin contain this carboxyl triad (for a sequence alignment, see ref Main, A. L., Harvey, T. S., Baron, M., Boyd, J. & Campbell, I. D. (1992) Cell 71, 671-678). The carboxyl triad of FNfn10 may be involved in important interactions that have not been identified to date.